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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,234	10/30/2003	Deirdre R. Meldrum	UW/Meldrum	2313

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EXAMINER
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LEVKOVICH, NATALIA A

ART UNIT	PAPER NUMBER
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1743

DATE MAILED: 01/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/698,234	MELDRUM ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Natalia Levkovich	1743	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 October 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being unclear for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites a 'method of preparing and handling protein samples for x-ray crystallography studies of protein crystals in the samples, comprising: providing a capillary tube having a sidewall and open ends; introducing plural fluid segments into the capillary tube; closing the ends of the capillary tube to seal the tube; and viewing and evaluating the fluid segments while they are in the sealed tube'. It is unclear what method steps are specifically directed to x-ray crystallography sample handling.

Claim 13 recites the 'method of claim 1, comprising introducing the fluid segments in the capillary tube by injecting them in through a first end of the tube, and providing plural ejectors, each ejecting a different fluid segment, and moving the first end of the tube into alignment with a first ejector, and operating the injector to introduce a fluid segment of its fluid into the first end of the tube, and then moving the first end of the tube into alignment with a second injector, and operating the second ejector to inject a fluid segment of its fluid into the first end of the tube'. It appears that the terms

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'injector' and 'ejector' refer to the same device. Clarification and consistent use of terms is requested.

Claim 21 recites fluid segments including 'a pair of axially spaced fluid segments that are separated by an air gap'. The term 'axially spaced' is indefinite in the given context, since 'axially' means both 'along an axis' and 'around an axis'.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-5, 9-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over David et al. (US 20020189529).

With respect to claims 1, 4-5, 9, 13-15, 20-21 and 23, David discloses a method for determining conditions for protein crystallization. A plurality of different crystallization

samples is introduced into “enclosed microvolumes” 100 [also referred to as “lumens”, channels, or grooves which equates to capillaries to be provided for the method– Ex.], as illustrated in Figure 1. A series of “crystallization conditions could be injected into the microlumen, alternating with suitable injections of material to be crystallized [‘fluid segments’ – Ex.] - ( See Abstract; [0116]). “ The dividers can be impermeable, semipermeable or permeable. For example, semipermeable substances such as air, oil, solvent, gel and beads can be used as dividers. The dividers can also be physical constructions, such as a narrow pore, a thin passage, a frit or sintered beads or powders”([0106]). “As shown in step A of FIG. 2, an enclosed lumen 201 is provided such that the lumen 201 has at least one opening 202A adjacent a first end of the lumen and at least one opening 202B adjacent a second end of the lumen. A crystallization experiment 203 is introduced into the lumen 201 via one of the openings, as shown in step B.... Step C of the figure shows the crystallization experiment proceeding ... If a crystal forms, as shown in step D of the figure (shown as 205), then the crystal may be examined in situ [‘viewing and evaluating’ – Ex.], for example, as shown in steps E-H. Examination may be performed by any available method, including... direct exposure of x-rays”([0093] – [0094]).

David does not specify closing the ends of a capillaries, however, David does teach that the “method has the advantages of ... tightly enclosed fluids to minimize evaporation”. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have employed a step of closing the ends of capillaries, in the modified method of David, in order to further curtail the evaporation.

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Referring to claims 2-3, David teaches that , “for ease of detection and fabrication, the entire device may be fabricated from a plastic material that is optically transparent...”([0079]).

Considering claim 10, David teaches applying vacuum to capillaries for introducing samples – see [0097], [0144], [0150].

As to claims 13-14, although David teaches sample introduction by ‘suitable alternating injections’, the reference does not specify employing dedicated injectors for different fluids. However, it would have been within the skill of the art, to employ dedicated injectors in the modified method of David, in order to speed up the step of sample introduction and for the ease of equipment maintenance.

6. Claims 6 and 24 rejected under 35 U.S.C. 103(a) as being unpatentable over David in view of Kimel (US 6551464).

David does not teach ‘closing the ends of the capillary tube by heating and pinching the sidewall of the tube at the ends of the tube’. However this method of sealing the tubes is known in the art for a very long time. For example, Kimel discloses glass tubes 16 and 18 being pinched (after the step of fluid introduction has been completed) to form a constriction 17 allowing to keep samples in the tube (Col.2, lines 45-60). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have employed heating / pinching the ends of capillaries, in the modified method of David, in order to further curtail the evaporation and keep samples in sample carriers.

7. Claims 7-8 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over David in view of Weigl et al. (US 20020025279).

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David does not teach 'closing the ends of the capillary tube by use of closure members (such as caps). However, these means of sealing the tubes are routinely used in the art. See, for example, Figures 9-10 in the Weigl reference, showing cap 80 and capillary 54. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have employed caps or other tube closures, in the modified method of David, in order to reduce the evaporation and keep samples in sample carriers.

8. Claims 11-12 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over David in view of McDevitt et al. (US 20020160363).

David does not teach a sealed vacuum chuck between the tube and the vacuum source. However these vacuum means are common in the art. See, for example, [0103] and Figures 72 A-D in the McDevitt reference. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have employed a sealed vacuum chuck in the modified method of David, in order to provide necessary vacuum.

9. Claims 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over David in view of Corbett et al. (US 5270183).

Although David does teach changing temperature condition during the process of growing crystals in [0006], the reference does not specifically disclose the step of cooling / freezing the samples. However, it is well known that crystallization process, in most cases, requires, first, heating and then cooling / freezing substances. Additionally, Corbett discloses segmented samples held in capillary tubes being periodically subjected to cooling. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have employed the steps of cooling / freezing the

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samples in the modified method of David, in order to provide necessary conditions for crystal growth, sample preservation and sample stability.

***Conclusion***

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Natalia Levkovich whose telephone number is 571-272-2462. The examiner can normally be reached on Mon-Fri, 8 a.m.-4p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
**YELENA GAKH  
PRIMARY EXAMINER**